September 13, 1949.

Dr. G. J. E. Thijsse,
Lab. Gezondheidsleer,
Mauritskade 57, (Oesterpark),
Amsterdam.

Dear Dr. Thijsse:

I have your inquiry concerning my doctoral dissertation. The dissertation has been filed with the Library of Yale University, which would be glad to receive your order for a microfilm copy. I am sorry that I do not have a copy available for loan. However, the dissertation contains very little beyond the material presented in my paper in <u>Genetics</u>, 1947, which you must already have seen. If you must have a detailed account, I would recommend that you ask Yale University for microfilms only of pp. 26-29 which bear a detailed derivation of the relationship between map distance and triple crossing-over. However, this can be briefly summarized:

Let x= map distance; r= recombination fraction [See Owen, Proc. Roy. Soc. London, B136: 67- (1949)]/

If we assume no interference, $2r = 1 - e^{-2x}$ or $r = e^{-x} \sinh x$.
This is true for a long segment (e.g. between [B,M] and [T,L]) x, or for any of its parts x_1, x_2, etc. The single crossover types of frequency (experimental) r_1, r_2, etc. are given by:

$$r_1 = \frac{(e^{-x_1} \sinh x_1)(e^{-x_2} \sinh x_2)(e^{-x_3} \cosh x_3)}{e^{-x} \sinh x}$$

etc.,. As $x_1 + x_2 + x_3 = x$, the exponential terms cancel out.

We also have for the frequency of the "triple crossover" prototrophs:

$$r_t = \frac{\sinh x_1 \sinh x_2 \sinh x_3}{\sinh x.}$$

Combining the four equations, we derive the cyclical set:

$\tanh x_1 = [r_1 . r_t / r_2 . r_3]^{1/2}$ from which the values given in the paper were derived. I leave to you the inference that it does not matter whether one implies a 2- or a 4-strand system.

Please let me know if I can be of any additional help. If you are working on bacterial recombination, I would be delighted to hear of your research.

Yours sincerely,

Joshua Lederberg
Assistant Professor of Genetics